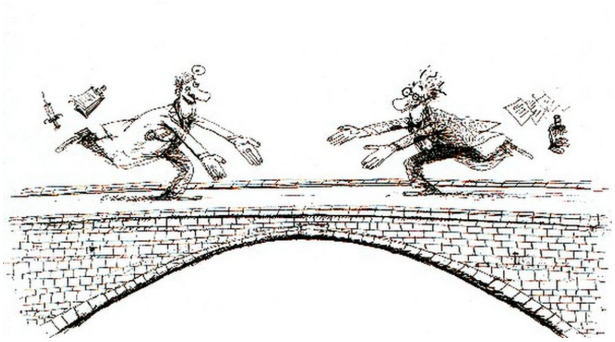

Demystifying Medicine
Speaker Profile

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Brief Biography and Research Summary

Dr. Hanover carried out his doctoral research with Dr. William J. Lennarz at Johns Hopkins University School of Medicine detailing the steps in the transmembrane assembly of membrane and secrretory proteins. He then did a Jane Coffin Childs postdoctoral fellowship with Dr. Ira H. Pastan focused on growth factor signaling, endocytosis and the molecular basis of drug resistance. In his independent work, he has pursued (1) the mechanism of nuclear transport and (2) the molecular features of a novel, glycan-dependent, signal-transduction cascade. The nuclear transport of transcription factors, nuclear kinases, steroid hormone receptors, and replication factors often serves a critical regulatory function. He explored the mechanisms of nuclear import, export, and subnuclear targeting. He also identified a novel nuclear transport pathway involving calmodulin. This pathway has been shown to play a role in mammalian sex determination and stem cell differentiation. The nuclear pore complex (NPC) mediates the transport of mRNA and proteins across the nuclear envelope. Dr. Hanover first identified the nuclear pore proteins and then cloned the first of these proteins, NUP62. Many components of the nuclear pore are modified by a novel modification: O-linked N-acetylglucosamine (O-linked GlcNAc). The modification also occurs on transcription factors and certain oncogenes and tumor suppressors. Dr. Hanover purified and cloned the human O-GlcNAc transferase (OGT). Based on its substrate specificity and molecular features, the Hanover lab proposed that O-linked GlcNAc transferase is the terminal step in a glucose-responsive pathway that becomes disregulated in diabetes mellitus (NIDDM). The enzyme catalyzing O-GlcNAc removal, O-GlcNAcase, has also been identified, expressed and shown to exist as differentially targeted isoforms in man. He continues to use genetically amenable Mouse, *C. elegans* and *Drosophila* models to examine the physiological impact of the enzymes of O-GlcNAc cycling. Using reverse genetics, knockout, and other transgenic models he is currently exploring the role of these essential genes in signal transduction and epigenetic regulation. O-GlcNAc has emerged as a key epigenetic regulator that may function in the intrauterine environment to influence disease susceptibility in the offspring. The enzymes of O-GlcNAc cycling also interact with key components of the machinery influencing DNA methylation associated with Genomic imprinting.

Selected Publications

1. Keembiyehetty, C., Love, D. C., Harwood, K. R., Gavrilova, O., Comly, M. E., and Hanover, J. A. 2015 Conditional knockout reveals a requirement for O-GlcNAcase in metabolic homeostasis., *J Biol Chem* January 16, 2015, doi: 10.1074/jbc.M114.617779
2. Olivier-Van Stichelen, S., and Hanover, J. A. 2014 X-inactivation normalizes O-GlcNAc transferase levels and generates an O-GlcNAc-depleted Barr body., *Front Genet* ***5***, 256. [PMC4120696]

3. Olivier-Van Stichelen, S., Abramowitz, L. K., and Hanover, J. A. 2014 X marks the spot: does it matter that O-GlcNAc transferase is an X-linked gene?, *Biochem Biophys Res Commun* ***453***, 201-207. [PMC4253714.

4. Abd-Elmoniem, K. Z., Bakalov, V. K., Matta, J. R., Muldoon, N., Hanover, J. A., Bondy, C. A., and Gharib, A. M. 2014 X chromosome parental origin and aortic stiffness in turner syndrome., *Clin Endocrinol (Oxf)* ***81***, 467-470.

5. Kim, E. J., Abramowitz, L. K., Bond, M. R., Love, D. C., Kang, D. W., Leucke, H. F., Kang, D. W., Ahn, J. S., and Hanover, J. A. 2014 Versatile O-GlcNAc transferase assay for high-throughput identification of enzyme variants, substrates, and inhibitors., *Bioconjug Chem* ***25***, 1025-1030. [PMC4215860]

6. Lewis, B. A., and Hanover, J. A. 2014 O-GlcNAc and the epigenetic regulation of gene expression., *J Biol Chem* ***289***, 34440-34448. [PMC4263851]

7. Harwood, K. R., and Hanover, J. A. 2014 Nutrient-driven O-GlcNAc cycling - think globally but act locally., *J Cell Sci* ***127***, 1857-1867. [PMC4004970]

8. Vigetti, D., Deleonibus, S., Moretto, P., Bowen, T., Fischer, J. W., Grandoch, M., Oberhuber, A., Love, D. C., Hanover, J. A., Cinquetti, R., Karousou, E., Viola, M., D'Angelo, M. L., Hascall, V. C., De Luca, G., and Passi, A. 2014 Natural antisense transcript for hyaluronan synthase 2 (HAS2-AS1) induces transcription of HAS2 via protein O-GlcNAcylation., *J Biol Chem* ***289***, 28816-28826. [PMC4200242]

9. Ghosh, S. K., Bond, M. R., Love, D. C., Ashwell, G. G., Krause, M. W., and Hanover, J. A. 2014 Disruption of O-GlcNAc Cycling in C. elegans Perturbs Nucleotide Sugar Pools and Complex Glycans., *Front Endocrinol (Lausanne)* ***5***, 197. [PMC4241842]

10. Bond, M. R., Ghosh, S. K., Wang, P., and Hanover, J. A. 2014 Conserved nutrient sensor O-GlcNAc transferase is integral to C. elegans pathogen-specific immunity., *PLoS One* ***9***, e113231. [PMC4256294]

11. Abramowitz, L. K., Olivier-Van Stichelen, S., and Hanover, J. A. 2014 Chromosome imbalance as a driver of sex disparity in disease., *J Genomics* ***2***, 77-88. [PMC4091450]

12. Kim, E. J., Bond, M. R., Love, D. C., and Hanover, J. A. 2014 Chemical tools to explore nutrient-driven O-GlcNAc cycling., *Crit Rev Biochem Mol Biol* ***49***, 327-342.

13. Kim, E. J., Kang, D. W., Leucke, H. F., Bond, M. R., Ghosh, S., Love, D. C., Ahn, J. S., Kang, D. O., and Hanover, J. A. 2013 Optimizing the selectivity of DIFO-based reagents for intracellular bioorthogonal applications., *Carbohydr Res* ***377***, 18-27.

14. Bond, M. R., and Hanover, J. A. 2013 O-GlcNAc cycling: a link between metabolism and chronic disease., *Annu Rev Nutr* ***33***, 205-229.

15. Hanover, J. A., and Wang, P. 2013 O-GlcNAc cycling shows neuroprotective potential in C. elegans models of neurodegenerative disease., *Worm* ***2***, e27043. [PMC3917942]